AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 16, line 35, with the following rewritten paragraph:

Bone enhancing agents, known in the art to increase bone formation, bone density or bone mineralisation, or to prevent bone resorption may be used in the methods and pharmaceutical compositions of the invention. Suitable bone enhancing agents include natural or synthetic hormones, such as estrogens, androgens, calcitonin, prostaglandins and parathormone; growth factors, such as platelet-derived growth factor, insulin-like growth factor, transforming growth factor, epidermal growth factor, connective tissue growth factor and fibroblast growth factor; vitamins, particularly vitamin D; minerals, such as calcium, ~~aluminum strontium~~ aluminum, strontium and fluoride; statin drugs, including pravastatin, fluvastatin, simvastatin, lovastatin and atorvastatin; ~~agonsists or antagonsist~~ agonists or antagonists of receptors on the surface of osteoblasts and osteoclasts, including parathormone receptors, estrogen receptors and prostaglandin receptors; biphosphonates and anabolic bone agents.

Please replace the paragraph beginning on page 18, line 8, with the following rewritten paragraph:

We used control groups in each ~~assays~~ assay to show that the assays were capable of detecting the effect of inhibition (bone resorption assay and osteoclast differentiation assay) or activation (osteoblast differentiation and bone formation). The control substances used were:

Bafilomycin A1 (in bone resorption assay)

~~17-β estradiol~~ 17β-estradiol (in osteoblast differentiation assay and bone formation assay)

Please replace the paragraph beginning on page 25, line 24, with the following rewritten paragraph:

8-10 week old mice were killed with CO_2. Tibia and femora were dissected free from adhering soft tissues. The bone ends were cut off with a scalpel and the marrow was flushed with α-Minimal Essential Medium (α-MEM, Gibco BRL, Paisley, UK) supplemented with 100 IU/ml penicillin and 100 µg/ml streptomycin. A 10ml syringe with a 27 gauge needle was used for flushing. Cells were centrifuged at 600 x G for 10 minutes and the cell pellet was resuspended in α-MEM containing 10% fetal calf serum. Cells were allowed to attach to plastic for 2 h at 37°C in a 5% CO_2 incubator to allow removal of monocytes and macrophages. Nonadherent cells were duly removed, and the attached bone marrow cells were cultured in 24-well plates (1×10^6 cells/well = 1ml) for 6 days. Half of the media changed at day 3 and the treatments replaced. At the end of the culture, the plates were fixed with 2 % paraformaldehyde in PBS for 20 minutes. Osteoclast formation was determined by measuring TRAP activity from the culture media using the novel TRAP immunoassay (*vide infra*), where we used polyclonal TRAP antiserum prepared in rabbits against purified human bone TRAP. The TRAP antibody was bound to anti-rabbit IgG coated mircotiter wells (Gibco BRL, Paisley, UK), and medium TRAP was then bound to the antibody. The activity of bound TRAP was measured in sodium acetate buffer using pNPP as substrate.

Please replace the paragraph beginning on page 35, line 7, with the following rewritten paragraph:

The lanthanum (III) ion showed a clear dose-dependent response in the osteoblast differentiation assay. The highest test concentrations (LA 5000 and LA 15000) inhibited, and the lowest test concentration (LA 100) activated osteoblast differentiation significantly. No significant response was observed with LA 500 and LA 1000. The control substance, ~~17-estradiol~~ 17β-estradiol, activated osteoblast differentiation significantly.

Please replace the paragraph beginning on page 40, line 5, with the following rewritten paragraph:

All concentrations of the lanthanum (III) ion tested showed a highly significant activation of the bone formation activity of mature osteoblasts, the activation being highest with the

highest test concentrations. The control substance, ~~17 estradiol~~ 17β-estradiol, activated bone formation significantly.

Please replace the paragraph beginning on page 41, line 11, with the following rewritten paragraph:

The mean and standard deviation (SD) of each group was determined. One-way analysis of variance (ANOVA) was used to study if the value obtained between different groups (baseline vs. controls and test substances) were statistically different (with $p < 0.05$). Statistical significance is shown in each table and figure with asterisks, one asterisk (*) indicating a p-value between 0.05 and 0.01, two asterisks (**) a p-value between 0.01 and 0.001, and three asterisks (***) ~~a p-value K 0.001~~ a p-value < 0.001. No asterisks indicate that the results of the group do not differ significantly from the results of the corresponding baseline group.

Please replace the paragraph beginning on page 43, line 12, with the following rewritten paragraph:

The specimens taken from the iliac crest of growing immature dogs were analysed. The group was divided into a control and treatment group. The treatment group received 1000 mg/Kg~~/day~~ of lanthanum carbonate administered orally twice daily. The groups were run for 13 weeks, after which time samples of bone were taken vertically through the iliac crest, embedded in methyl methacrylate based resin, sectioned and stained with toluidine blue and Von Kossa stain. The parameters measured were:

- Trabecular and cortical bone mass
- Osteoid surface and volume
- Osteoblast surface
- Cortical osteoid volume
- Trabecular and cortical osteoclast number
- Resorptive surfaces in cortex and trabecular bone
- ~~Incorporation of lanthanum within bone (modified solochrome azurine technique)~~